08/442,288

```
=> s vaccine
L1         2998 VACCINE

=> s adjuvant
L2        12098 ADJUVANT

=> s l1 and l2
L3         1213 L1 AND L2

=> s saponin and l3
           2534 SAPONIN
L4           95 SAPONIN AND L3

=> s mpl and l4
            176 MPL
L5            3 MPL AND L4

=> d l5 ab cit 1-3
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US PAT NO: 5,356,622 [IMAGE AVAILABLE] L5: 1 of 3

ABSTRACT:
A vaccine for protecting avian and mammalian subjects against flea infestation comprises the supernatant fraction of flea midgut, or the antigenic components thereof. This also has the effect of reducing flea populations in the environment of the subject. Antibodies raised by these vaccines are also useful in purification and diagnosis.

1. 5,356,622, Oct. 18, 1994, Flea midgut-supernatant vaccines; Andrew W. Heath, et al., 424/265.1; 514/830; 530/427, 858 [IMAGE AVAILABLE]

US PAT NO: 5,338,543 [IMAGE AVAILABLE] L5: 2 of 3

ABSTRACT:
The invention relates to a method for making an inactivated vaccine of Mycoplasma hyopneumoniae by inactivating the bacteria with Thimerosal. The resulting bacterin is mixed with an adjuvant of aluminum hydroxide and DEAE dextran and injected into pigs. The resulting bacterin and adjuvant mixture can also be mixed with other bacteria such as Borderella and Pasteurella, for further adjuvant effect. Protective immunity against mycoplasmal pneumonia is elicited in swine using these vaccines.

2. 5,338,543, Aug. 16, 1994, Thimerosal inactivated mycoplasma hyopneumoniae vaccine ; Gerald R. Fitzgerald, et al., 424/264.1, 825; 435/252.1, 870 [IMAGE AVAILABLE]

US PAT NO: 5,273,744 [IMAGE AVAILABLE] L5: 3 of 3

ABSTRACT:
This invention relates to the development of a vaccine against Theileria parva, which is a protozoan parasite infecting cattle in Africa. The invention specifically relates to the use of the 67 kDa glycoprotein from the surface of the T. parva sporozoite as an immunogen for inducing immunoprotection against T. parva in bovine species. This 67 kDa antigen is produced using recombinant genetics. Plasmids containing nucleic acid segments encoding the antigen, host cells containing the nucleic acid segments and recombinant methods for producing the antigen are part of this invention.

3. 5,273,744, Dec. 28, 1993, Vaccines for the protection of animals against theileria infection; Anthony J. Musoke, et al., 424/191.1, 266.1, 269.1; 435/69.3; 530/350, 395, 806; 536/23.7; 930/210 [IMAGE AVAILABLE]

=> d his

(FILE 'USPAT' ENTERED AT 15:49:59 ON 19 JUL 95)

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L1          2998 S VACCINE
L2         12098 S ADJUVANT
L3          1213 S L1 AND L2
L4            95 S SAPONIN AND L3
L5             3 S MPL AND L4

=> s monophosphoryl(4w)lipid(4w)a
            37 MONOPHOSPHORYL
          9237 LIPID
       1802477 A
L6            31 MONOPHOSPHORYL(4W)LIPID(4W)A

=> s l3 and l6
L7            13 L3 AND L6

=> s l4 and l7
L8             1 L4 AND L7

=> d l8 ab cit 1
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US PAT NO: 5,356,622 [IMAGE AVAILABLE] L8: 1 of 1

ABSTRACT:
A vaccine for protecting avian and mammalian subjects against flea infestation comprises the supernatant fraction of flea midgut, or the antigenic components thereof. This also has the effect of reducing flea populations in the environment of the subject. Antibodies raised by these vaccines are also useful in purification and diagnosis.

1. 5,356,622, Oct. 18, 1994, Flea midgut-supernatant vaccines; Andrew W. Heath, et al., 424/265.1; 514/830; 530/427, 858 [IMAGE AVAILABLE]

=> d l7 cit 1-13

1. 5,372,928, Dec. 13, 1994, Hepatitis C virus isolates; Tatsuo Miyamura, et al., 435/5, 6; 536/23.72, 24.32; 935/8, 9, 78 [IMAGE AVAILABLE]

2. 5,356,622, Oct. 18, 1994, Flea midgut-supernatant vaccines; Andrew W. Heath, et al., 424/265.1; 514/830; 530/427, 858 [IMAGE AVAILABLE]

3. 5,350,842, Sep. 27, 1994, DNAs encoding Treponema pallidum antigens; Michael V. Norgard, 536/23.7; 435/252.3 [IMAGE AVAILABLE]

4. 5,350,671, Sep. 27, 1994, HCV immunoassays employing C domain antigens; Michael Houghton, et al., 435/5, 6, 975; 436/512, 518; 530/300, 326, 327, 328, 812, 826; 930/220, 223 [IMAGE AVAILABLE]

5. 5,340,588, Aug. 23, 1994, Liposphere carriers of vaccines; Abraham J. Domb, 424/450, 193.1, 812 [IMAGE AVAILABLE]

6. 5,185,147, Feb. 9, 1993, Short polypeptide sequences useful in the production and detection of antibodies against human immunodeficiency

virus; Lawrence D. Papsidero, 424/188.1, 208.1; 435/240.27; 514/13, 14, 15, 16, 17; 530/326, 327, 328, 329, 387.2, 387.9, 388.35, 402, 403, 826; 930/221 [IMAGE AVAILABLE]

7. 5,171,568, Dec. 15, 1992, Recombinant herpes simplex gb-gd vaccine ; Rae L. Burke, et al., 424/186.1, 231.1, 279.1, 283.1, 450, 812; 435/69.3, 172.3, 235.1, 320.1; 514/8; 536/23.72 [IMAGE AVAILABLE]

8. 5,156,949, Oct. 20, 1992, Immunoassays for antibody to human immunodeficiency virus using recombinant antigens; Paul A. Luciw, et al., 435/5, 7.2, 69.1, 172.3, 252.33, 810, 820, 974; 935/60, 66, 69, 71 [IMAGE AVAILABLE]

9. 5,026,557, Jun. 25, 1991, Adjuvant composition; Leonard Estis, et al., 424/450, 184.1, 193.1, 277.1, 283.1, 812 [IMAGE AVAILABLE]

10. 5,013,555, May 7, 1991, Agent for desensitizing man and/or animals against an allergen; Amy L. T. Collins, 424/450, 195.1, 539, 542, 688; 514/885 [IMAGE AVAILABLE]

11. 4,975,420, Dec. 4, 1990, Agents and procedures for provoking an immune response to GnRH and immuno sterilizing mammals; David W. Silversides, et al., 424/195.11, 198.1, 278.1, 279.1, 280.1, 283.1, 811; 514/15, 800; 530/313, 328 [IMAGE AVAILABLE]

12. 4,912,094, Mar. 27, 1990, Modified lipopolysaccharides and process of preparation; Kent R. Myers, et al., 514/54; 435/101; 536/1.11, 4.1, 17.1, 115, 117, 119, 124 [IMAGE AVAILABLE]

13. 4,877,611, Oct. 31, 1989, Vaccine containing tumor antigens and adjuvants; John L. Cantrell, 424/277.1, 278.1, 282.1; 514/885, 937, 938, 939, 943 [IMAGE AVAILABLE]

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=> s t(4w)cell
        419631 T
        156311 CELL
L9        4121 T(4W)CELL

=> s gamma(4w)inteferon
         74909 GAMMA
            63 INTEFERON
L10          8 GAMMA(4W)INTEFERON

=> s l10 and l9
L11          2 L10 AND L9

=> d l11 cit 1-2
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1. 4,897,264, Jan. 30, 1990, Human gamma interferon-specific receptor protein, antibody against said protein, methods for obtaining said protein and said antibody and compositions containing said protein and antibody; Daniela Novick, et al., 424/85.5; 435/183 [IMAGE AVAILABLE]

2. 4,771,125, Sep. 13, 1988, Human soluble immune response suppressor; H. William Schnaper, et al., 530/351; 435/70.4; 530/350, 412, 416, 417, 418, 420 [IMAGE AVAILABLE]

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=> e prieels, john p./in
E1           4     PRIEELS, JEAN PAUL/IN
E2           1     PRIEELS, JEAN PAUL H P/IN
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E3            0 --> PRIEELS, JOHN P/IN
E4            1     PRIEFER, URSULA/IN
E5            1     PRIEFERT, ERWIN E/IN
E6            1     PRIEFERT, LONNIE E/IN
E7            1     PRIEFERT, MARVIN H/IN
E8            7     PRIEFERT, MARVIN J/IN
E9            8     PRIEFERT, WILLIAM D/IN
E10           4     PRIEGEL, JACK C/IN
E11          17     PRIEGNITZ, JAMES W/IN
E12           1     PRIEGNITZ, JAMES WILLIAM/IN

=> d his

     (FILE 'USPAT' ENTERED AT 15:49:59 ON 19 JUL 95)
L1         2998 S VACCINE
L2        12098 S ADJUVANT
L3         1213 S L1 AND L2
L4           95 S SAPONIN AND L3
L5            3 S MPL AND L4
L6           31 S MONOPHOSPHORYL(4W)LIPID(4W)A
L7           13 S L3 AND L6
L8            1 S L4 AND L7
L9         4121 S T(4W)CELL
L10           8 S GAMMA(4W)INTEFERON
L11           2 S L10 AND L9
                E PRIEELS, JOHN P./IN

=> s l10 and l3
L12           0 L10 AND L3

=> s l9 and l3
L13         276 L9 AND L3

=> s l13 and l10
L14           0 L13 AND L10

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J IMMUNOL 146 (2). 1991. 431-437. CODEN: JOIMA
Full Journal Title: Journal of Immunology
Language: ENGLISH

Saponins were purified from Quillaja saponaria Molina bark by silica and reverse phase chromatography. The resulting purified saponins were tested for adjuvant activity in mice. Several distinct saponins, deisgnated QS-7, QS-17, QS-18, and QS-21, were demonstrated to boost antibody levels by 100-fold or more when used in mouse immunizations with the Ag BSA and beef liver cytochrome B5. These purified saponins increased titers in all major IgG subclasses. To determine optimal dose in mice for adjuvant response, QS-7 and QS-21 were tested in a dose-response study in intradermal immunization with BSA in mice; for both of these purified saponins, adjuvant response (determined by stimulation of ELISA titers to BSA) near maximum at doses of 5 .mu.g and was shown to plateau up to the highest dose

tested, 80 .mu.g. These purified saponins vary considerably in their toxicity, as assessed by lethality in mice; the main component, QS-18, being the most toxic. Saponins QS-7 and QS-21 showed no or very low toxicity in mice, respectively. None of these saponins stimulated production of reaginic antibodies. The monosaccharide composition of these saponins showed similar but distinct compositions with all four containing fucose, xylose, galactose, and glucuronic acid. Predominant differences were observed in the quantities of rhamnose, arabinose, and glucose. Monomer m.w. (determined by size exclusion HPLC) were determined to range from 1800 to 2200.

Descriptors/Keywords: MOUSE IMMUNOGLOBULIN G TOXICITY MONOSACCHARIDE COMPOSITION VACCINE FORMULATION CHROMATOGRAPHY

Concept Codes:

*10068	Biochemical Studies-Carbohydrates
*10506	Biophysics-Molecular Properties and Macromolecules
*13012	Metabolism-Proteins, Peptides and Amino Acids
*22018	Pharmacology-Immunological Processes and Allergy
*22504	Toxicology-Pharmacological Toxicology (1972-)
*34502	Immunology and Immunochemistry-General; Methods
*54000	Pharmacognosy and Pharmaceutical Botany
10056	Biochemical Methods-Lipids
10058	Biochemical Methods-Carbohydrates
10064	Biochemical Studies-Proteins, Peptides and Amino Acids
10066	Biochemical Studies-Lipids
10504	Biophysics-General Biophysical Techniques
34504	Immunology and Immunochemistry-Bacterial, Viral and Fungal
36001	Medical and Clinical Microbiology-General; Methods and Techniques
51522	Plant Physiology, Biochemistry and Biophysics-Chemical Constituents

Biosystematic Codes:

26675	Rosaceae
86375	Muridae

Super Taxa:

Plants; Vascular Plants; Spermatophytes; Angiosperms; Dicots; Animals; Chordates; Vertebrates; Nonhuman Vertebrates; Mammals; Nonhuman Mammals ; Rodents

13/5/2 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09330529 95260529

Effect of adjuvants on immunogenicity of MN recombinant glycoprotein 120 in guinea pigs.

Powell MF; Eastman DJ; Lim A; Lucas C; Peterson M; Vennari J; Weissburg RP; Wrin T; Kensil CR; Newman MJ; et al

Department of Pharmaceutical Research, Genentech, Inc., South San Francisco, California 94080, USA.

AIDS Res Hum Retroviruses (UNITED STATES) Feb 1995, 11 (2) p203-9, ISSN 0889-2229 Journal Code: ART

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9508

Subfile: INDEX MEDICUS

The immunogenicity of recombinant gp120 from the MN strain of HIV-1, a candidate HIV-1 vaccine, was evaluated in guinea pigs using adjuvant formulations with different physical and chemical properties. The adjuvants tested included Freund's adjuvant (FA), alum, and the novel adjuvant QS-21.

These studies demonstrated that QS-21 provides a number of advantages compared to the two other adjuvants tested. QS-21 formulations accelerated the production of antibodies to MN rgp120 and elicited complete seroconversion after a single immunization. QS-21 shifted the antigen dose-response curve for antibody production by as much as three orders of magnitude, enabling a more economical use of antigen. Antibody titers to MN rgp120 and to the principal neutralizing determinant in the V3 domain were higher in animals receiving QS-21 formulations than in animals immunized with the other adjuvants, and correlated well with higher virus neutralization titers in an in vitro assay. These results support the testing of QS-21 in future clinical trials of candidate HIV-1 vaccines.

Tags: Animal; Comparative Study; Human

Descriptors: *Adjuvants, Immunologic--Pharmacology--PD; *HIV Envelope Protein gp120--Immunology--IM; *Saponins--Pharmacology--PD; Amino Acid Sequence; Antibody Formation--Drug Effects--DE; AIDS Vaccines --Administration and Dosage--AD; CHO Cells; Guinea Pigs; Hamsters; HIV Envelope Protein gp120--Administration and Dosage--AD; Molecular Sequence Data; Recombinant Proteins--Immunology--IM

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Envelope Protein gp120); 0 (Recombinant Proteins); 0 (Saponins); 141256-04-4 (QS 21)

13/5/3 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09291963 95221963

Protection of dogs from Lyme disease with a vaccine containing outer surface protein (Osp) A, OspB, and the saponin adjuvant QS21.

Coughlin RT; Fish D; Mather TN; Ma J; Pavia C; Bulger P

Cambridge Biotech Corp., Worcester, Massachusetts 01605.

J Infect Dis (UNITED STATES) Apr 1995, 171 (4) p1049-52, ISSN 0022-1899 Journal Code: IH3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9507

Subfile: AIM; INDEX MEDICUS

A vaccine consisting of purified Escherichia coli-expressed recombinant full-length outer surface proteins A (OspA) and B (OspB) and the saponin adjuvant QS21 was evaluated for protection against Borrelia burgdorferi infection. Eleven beagles were vaccinated twice and then challenged with 10 field-collected adult female Ixodes scapularis. Xenodiagnosis revealed that all 11 nonvaccinated control dogs and 2 of 10 vaccinated dogs were infected with B. burgdorferi. Six of 11 control dogs also developed fever (0.75 +/- 0.38 degrees C) and were lethargic. One of the control dogs also developed a limp. Both of the infected vaccinated dogs were asymptomatic. Thus, the vaccine prevented tick-vectored infection and associated symptoms of Lyme disease.

Tags: Animal; Female; Male; Support, Non-U.S. Gov't

Descriptors: *Adjuvants, Immunologic; *Antigens, Surface--Immunology--IM; *Bacterial Outer Membrane Proteins--Immunology--IM; *Bacterial Vaccines; *Borrelia burgdorferi--Immunology--IM; *Lyme Disease --Prevention and Control--PC; *Saponins--Immunology--IM; Antibodies, Bacterial--Biosynthesis --BI; Antibodies, Bacterial--Blood--BL; Bacterial Vaccines--Immunology--IM ; Borrelia burgdorferi--Isolation and Purification--IP; Dogs; IgG --Biosynthesis--BI; IgG--Blood--BL; Ticks--Microbiology--MI; Vaccination; Vaccines, Synthetic--Immunology--IM

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Antibodies, Bacterial); 0 (Antigens, Surface); 0 (Bacterial Outer Membrane Proteins)

; 0 (Bacterial Vaccines); 0 (IgG); 0 (OspA protein); 0 (Saponins); 0 (Vaccines, Synthetic); 141256-04-4 (QS 21); 149719-59-5 (OspB protein)

13/5/4 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09239484 95169484
Development of a single-shot subunit vaccine for HIV-1.
Cleland JL; Powell MF; Lim A; Barron L; Berman PW; Eastman DJ; Nunberg JH ; Wrin T; Vennari JC
Department of Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, California 94080.
AIDS Res Hum Retroviruses (UNITED STATES) 1994, 10 Suppl 2 pS21-6, ISSN 0889-2229 Journal Code: ART
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9506
Subfile: INDEX MEDICUS
The successful development of an AIDS vaccine will require formulations that not only invoke the desired immunological response, but also are stable and easy to administer. A single shot MN rgp120 vaccine formulation comprised of MN rgp120 encapsulated in poly (lactic-coglycolic) acid (PLGA) microspheres was developed to provide an in vivo autoboost of antigen. These formulations were designed to yield an in vivo autoboost at 1, 2, 3 or 4-6 months. In addition, PLGA microspheres containing the adjuvant, QS21, were also prepared to provide an in vivo autoboost concomitant with antigen. In guinea pigs, these formulations yielded higher anti-MN rgp120 and anti-V3 loop antibody titers than alum formulations that were administered at higher antigen doses. Different doses of encapsulated MN rgp120 provided a clear and well-defined dose response curve for both anti-MN rgp120 and anti-V3 loop antibody titers. When soluble QS21 was mixed with the encapsulated MN rgp120, the antibody titers were increased by a factor of 5 over the titers with encapsulated MN rgp120 alone. An additional fivefold increase in antibody titers was observed for guinea pigs immunized with encapsulated MN rgp120 and QS21 on the same microspheres. These results suggest that the adjuvant properties of QS21 can be increased by microencapsulation in PLGA. Furthermore, antibodies induced by these preparations neutralized the MN strain of HIV-1. The neutralization titers for sera from animals immunized with MN rgp120-PLGA and soluble QS21 were greater than the titers obtained from guinea pigs that were treated with MN rgp120 and soluble QS21 at the same dose. Overall, these studies validate the in vivo autoboost concept, reveal a method for improving the adjuvant properties of QS21, and indicate the potential of future single shot vaccine formulations.
Tags: Animal; Comparative Study; Human
Descriptors: *AIDS Vaccines--Isolation and Purification--IP; *HIV-1 --Immunology--IM; Adjuvants, Immunologic--Administration and Dosage--AD; Alum Compounds--Administration and Dosage--AD; AIDS Vaccines --Administration and Dosage--AD; Delayed-Action Preparations; Guinea Pigs; HIV Antibodies--Biosynthesis--BI; HIV Envelope Protein gp120 --Administration and Dosage--AD; HIV Envelope Protein gp120--Immunology --IM; HIV Envelope Protein gp120--Isolation and Purification--IP; Microspheres; Neutralization Tests; Peptide Fragments--Immunology--IM; Polymers--Administration and Dosage--AD; Saponins --Administration and Dosage--AD; Vaccines, Synthetic--Administration and Dosage--AD; Vaccines, Synthetic--Isolation and Purification--IP
CAS Registry No.: 0 (polylactic acid-polyglycolic acid copolymer); 0

(Adjuvants, Immunologic); 0 (Alum Compounds); 0 (AIDS Vaccines); 0 (Delayed-Action Preparations); 0 (HIV envelope protein gp120 (305-321)); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Peptide Fragments); 0 (Polymers); 0 (Saponins); 0 (Vaccines, Synthetic); 10043-01-3 (aluminum sulfate); 141256-04-4 (QS 21)

13/5/5 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09239463 95169463
Immunogenicity and HIV-1 virus neutralization of MN recombinant glycoprotein 120/HIV-1 QS21 vaccine in baboons.
Powell MF; Cleland JL; Eastman DJ; Lim A; Newman MJ; Nunberg JH; Weissburg RP; Vennari JC; Wrin T; Berman PW
Department of Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, California 94080.
AIDS Res Hum Retroviruses (UNITED STATES) 1994, 10 Suppl 2 pS105-8, ISSN 0889-2229 Journal Code: ART
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9506
Subfile: INDEX MEDICUS
The effect of adjuvant and immunization schedule on the immunogenicity of HIV-1 envelope glycoprotein, MN rgp120, was optimized by using baboons. The novel adjuvant QS21 elicited earlier seroconversion than alum adjuvant, and the antibody titers to MN rgp120 for animals treated with QS21 were significantly greater than the titers obtained in animals treated with alum. The use of QS21 shifted the dose-response curve, resulting in less MN rgp120 required to achieve equivalent titers to those in the alum formulations. The in vitro virus neutralizing (VN) titers from animals treated with QS21 were 3- to 10-fold higher than with alum. The data presented herein point to the superiority of QS21 as adjuvant in primates for MN rgp120.
Tags: Animal; Comparative Study; In Vitro
Descriptors: *AIDS Vaccines--Immunology--IM; *HIV-1--Immunology--IM; Adjuvants, Immunologic--Administration and Dosage--AD; Alum Compounds --Administration and Dosage--AD; AIDS Vaccines--Administration and Dosage --AD; HIV Antibodies--Biosynthesis--BI; HIV Envelope Protein gp120 --Administration and Dosage--AD; HIV Envelope Protein gp120--Immunology --IM; HIV Seropositivity--Immunology--IM; Neutralization Tests; Papio; Saponins--Administration and Dosage--AD; Saponins--Immunology--IM; Vaccines, Synthetic--Administration and Dosage--AD; Vaccines, Synthetic --Immunology--IM
CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Alum Compounds); 0 (AIDS Vaccines); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Saponins); 0 (Vaccines, Synthetic); 10043-01-3 (aluminum sulfate); 141256-04-4 (QS 21)

13/5/6 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09229643 95159643
Phase 1 trial of immunological adjuvant QS-21 with a GM2 ganglioside-keyhole limpet haemocyanin conjugate vaccine in patients with malignant melanoma.
Livingston PO; Adluri S; Helling F; Yao TJ; Kensil CR; Newman MJ;

Marciani D
Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.
Vaccine (ENGLAND) Nov 1994, 12 (14) p1275-80, ISSN 0264-410X
Journal Code: X60
Contract/Grant No.: CA 40532, CA, NCI
Languages: ENGLISH
Document type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE I; JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9505
Subfile: INDEX MEDICUS
Increasing doses of saponin fraction QS-21 were administered as immunological adjuvant in a Phase 1 trial with a constant dose of the melanoma ganglioside GM2 covalently attached to keyhole limpet haemocyanin (KLH). Twenty-eight patients with AJCC Stage III or IV melanoma who were free from disease after surgery were treated with six vaccinations administered subcutaneously over a 5-month period. Local and systemic reactions were QS-21 dose-related. Doses of < or = 100 micrograms induced mild local tenderness and inflammation at vaccination sites lasting 2-4 days and occasional brief low-grade fever and malaise, but no significant incapacitation. The 200 micrograms dose induced low-grade fever and malaise after 30% of vaccinations and local reactions as large as 20 cm in diameter were seen in all patients, resulting in discomfort with usage of the injected extremity for 5-10 days. The titres of IgM and IgG antibodies against GM2, and IgG antibodies against KLH, were highest at the 100 and 200 micrograms QS-21 doses. No antibodies against QS-21 were detected. This trial identifies the 100 micrograms dose of QS-21 as the optimal well tolerated dose for induction of antibodies against both the melanoma ganglioside/GM2 and the protein KLH in melanoma patients.
Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *Adjuvants, Immunologic--Pharmacology--PD; *G(M2) Ganglioside--Immunology--IM; *Hemocyanin--Immunology--IM; *Melanoma --Therapy--TH; *Saponins--Pharmacology--PD; Antibodies, Neoplasm --Biosynthesis--BI; Hypersensitivity, Delayed--Immunology--IM
CAS Registry No.: 0 (keyhole-limpet hemocyanin); 0 (Adjuvants, Immunologic); 0 (Antibodies, Neoplasm); 0 (Saponins); 141256-04-4 (QS 21); 19600-01-2 (G(M2) Ganglioside); 9013-72-3 (Hemocyanin)

13/5/7 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09166559 95096559
Formulation of an immunogenic human cytomegalovirus vaccine: responses in mice.
Britt W; Fay J; Seals J; Kensil C
Department of Pediatrics, University of Alabama at Birmingham 35233.
J Infect Dis (UNITED STATES) Jan 1995, 171 (1) p18-25, ISSN 0022-1899
Journal Code: IH3
Contract/Grant No.: AI-30105, AI, NIAID; AI-30290, AI, NIAID; HD-10699, HD, NICHD
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9503
Subfile: AIM; INDEX MEDICUS
The immunogenicity of a vaccine formulation consisting of recombinant-derived human cytomegalovirus (HCMV) glycoprotein B (UL55) combined with a chemically defined adjuvant derived from saponin, QS-21, was evaluated in mice. The immune responses of mice given the gB/QS-21 formulation were compared with those induced by gB combined with either

Freund's adjuvant or aluminum hydroxide. The gB/QS-21 combination induced higher levels of virus-binding antibodies and significantly higher levels of virus-neutralizing antibodies than gB combined with either Freund's adjuvant or aluminum hydroxide. Animals given gB/QS-21 exhibited IgG subclass switching and produced significant titers of virus-specific IgG2a antibodies. Furthermore, animals given gB/QS-21 produced antigen-specific cytotoxic spleen cells. Because of its immunogenicity, a subunit vaccine containing HCMV gB and QS-21 offers a potential approach to the immunoprophylaxis of HCMV disease.

Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Antibodies, Viral--Biosynthesis--BI; *Cytomegalovirus --Immunology--IM; *Saponins--Immunology--IM; *Viral Envelope Proteins --Immunology--IM; *Viral Vaccines--Immunology--IM; Adjuvants, Immunologic; Aluminum Hydroxide--Immunology--IM; Antibody Specificity; Cytomegalovirus Infections--Prevention and Control--PC; Cytotoxicity, Immunologic; Dose-Response Relationship, Immunologic; Freund's Adjuvant; Immunization, Secondary; Immunoglobulin Class Switching; Mice; Mice, Inbred BALB C; Neutralization Tests; Vaccination; Vaccines, Synthetic--Immunology--IM

CAS Registry No.: 0 (glycoprotein B, type 1 herpes simplex virus); 0 (Adjuvants, Immunologic); 0 (Antibodies, Viral); 0 (Saponins); 0 (Vaccines, Synthetic); 0 (Viral Envelope Proteins); 0 (Viral Vaccines) ; 141256-04-4 (QS 21); 21645-51-2 (Aluminum Hydroxide); 9007-81-2 (Freund's Adjuvant)

13/5/8 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09148004 95078004

Induction of antigen-specific killer T lymphocyte responses using subunit SIVmac251 gag and env vaccines containing QS-21 saponin adjuvant.

Newman MJ; Munroe KJ; Anderson CA; Murphy CI; Panicali DL; Seals JR; Wu JY; Wyand MS; Kensil CR

Cambridge Biotech Corporation, Worcester, Massachusetts 01605.

AIDS Res Hum Retroviruses (UNITED STATES) Jul 1994, 10 (7) p853-61, ISSN 0889-2229 Journal Code: ART

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9503

Subfile: INDEX MEDICUS

Subunit vaccines based on recombinant proteins have proved useful for inducing antibody responses and they are safe for widespread use because they do not contain any live components. Unfortunately, they do not typically induce the types of cell-mediated immune responses required to control viral pathogens; specifically, they do not induce CD8+ cytotoxic T lymphocyte (CTL) responses. To increase the immunogenicity of recombinant proteins, we have used the QS-21 saponin adjuvant in subunit vaccine formulations. In the current study, experimental subunit vaccine formulations containing recombinant p55gag or gp120env proteins from the mac251 strain of the simian immunodeficiency virus (SIVmac251) and the QS-21 adjuvant were used to immunize rhesus macaques. These formulations induced SIV gag- or env-specific cellular immunity that was detectable in vitro and included killer cell activity. The induction of killer cells required prior vaccination and the responses were antigen specific for the immunogens contained in the vaccine formulations. Autologous target cells were required to detect these responses, suggesting genetic restriction, and effector cells appeared to be present in both the CD4+ and CD8+ T lymphocyte subpopulations. These data suggest that the vaccine-induced killer cell activity that was detected was mediated by both CD4+ and CD8+

lymphocytes. Despite the presence of these killer cells, all of the animals became infected with the SIVmac251 on experimental challenge. These findings demonstrated that antigen-specific killer cell responses could be induced by a subunit vaccine formulated with the QS-21 saponin adjuvant. The characteristics of the responses suggested that the effector cells were T lymphocytes, expressing either CD4 or CD8.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Animal; Male

Descriptors: *CD4-Positive T-Lymphocytes--Pathology--PA; *CD8-Positive T-Lymphocytes--Pathology--PA; *Saponins--Administration and Dosage--AD; *Simian Acquired Immunodeficiency Syndrome--Prevention and Control--PC; *SAIDS Vaccines--Administration and Dosage--AD; *SIV--Pathogenicity--PY; Amino Acid Sequence; Genes, env--Immunology--IM; Genes, gag--Immunology--IM ; Lymph Nodes--Pathology--PA; Macaca mulatta; Molecular Sequence Data; Saponins--Immunology--IM; SAIDS Vaccines--Genetics--GE; SAIDS Vaccines --Immunology--IM; SIV--Genetics--GE; SIV--Immunology--IM; Vaccination

CAS Registry No.: 0 (Saponins); 0 (SAIDS Vaccines); 141256-04-4 (QS 21)

Gene Symbol: GAG; ENV

13/5/9 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08769693 94084693

GD3 vaccines for melanoma: superior immunogenicity of keyhole limpet hemocyanin conjugate vaccines.

Helling F; Shang A; Calves M; Zhang S; Ren S; Yu RK; Oettgen HF; Livingston PO

Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, New York 10021.

Cancer Res (UNITED STATES) Jan 1 1994, 54 (1) p197-203, ISSN 0008-5472 Journal Code: CNF

Contract/Grant No.: CA33049, CA, NCI; CA 08478, CA, NCI; NS-11853-19, NS, NINDS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9403

Subfile: INDEX MEDICUS

Cell surface gangliosides show altered patterns of expression as a consequence of malignant transformation and have therefore been of interest as potential targets for immunotherapy, including vaccine construction. One obstacle has been that some of the gangliosides that are overexpressed in human cancers are poorly immunogenic in humans. A case in point is GD3, a prominent ganglioside of human malignant melanoma. Using an approach that has been effective in the construction of bacterial carbohydrate vaccines, we have succeeded in increasing the immunogenicity of GD3 in the mouse by conjugating the ganglioside with immunogenic carriers. Several conjugation methods were used. The optimal procedure involved ozone cleavage of the double bond of GD3 in the ceramide backbone, introducing an aldehyde group, and coupling to aminolysyl groups of proteins by reductive amination. Conjugates were constructed with a synthetic multiple antigenic peptide expressing repeats of a malarial T-cell epitope, outer membrane proteins of Neisseria meningitidis, cationized bovine serum albumin, keyhole limpet hemocyanin, and polylysine. Mice immunized with these conjugates showed a stronger antibody response to GD3 than mice immunized with unconjugated GD3. The strongest response was observed in mice immunized with the keyhole limpet hemocyanin conjugate of the GD3 aldehyde derivative and the adjuvant QS-21. These mice showed not only a long-lasting high-titer IgM response

but also a consistent high-titer IgG response (predominantly IgG1), indicating recruitment of T-cell help, although the titers of IgM and IgG antibodies following booster immunizations were not as high as they are in the response to classical T-cell-dependent antigens. This method is applicable to other gangliosides, and it may be useful in the construction of immunogenic ganglioside vaccines for the immunotherapy of human cancers expressing gangliosides on their cell surface.

Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Gangliosides--Immunology--IM; *Immunotoxins--Immunology--IM; *Melanoma--Immunology--IM; *Oligosaccharides--Immunology--IM; *Vaccines--Immunology--IM; Adjuvants, Immunologic; Antibodies, Neoplasm--Immunology--IM; Gangliosides--Chemistry--CH; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Saponins--Immunology--IM; Vaccines--Chemistry--CH

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Antibodies, Neoplasm); 0 (Gangliosides); 0 (Immunotoxins); 0 (Oligosaccharides); 0 (Saponins); 0 (Vaccines); 141256-04-4 (QS 21); 62010-37-1 (ganglioside, GD3)

13/5/10 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08393829 93103829

Immunogenicity and toxicity testing of an experimental HIV-1 vaccine in nonhuman primates.

Newman MJ; Wu JY; Coughlin RT; Murphy CI; Seals JR; Wyand MS; Kensil CR
Cambridge Biotech Corporation, Worcester, MA 01605.

AIDS Res Hum Retroviruses (UNITED STATES) Aug 1992, 8 (8) p1413-8, ISSN 0889-2229 Journal Code: ART
Contract/Grant No.: U01-A128167
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9303
Subfile: INDEX MEDICUS

A highly purified saponin from Q. saponaria (QS-21) was tested in juvenile rhesus macaques for adjuvant activity and toxicity. The QS-21 was tested alone or as part of an experimental subunit HIV-1 vaccine containing a truncated recombinant HIV-1 envelope protein (gp160D) adsorbed to alum. Antibody responses were measured using ELISA and cell-mediated immunity was measured using cellular proliferation assays. Potential toxicity was monitored by standard clinical pathology testing using peripheral blood and urine samples. No toxic effects were observed, even after the administration of the experimental vaccines three times at monthly intervals. The QS-21 saponin adjuvant enhanced total antibody production levels by greater than 100-fold and broadened the specificity of the response so that additional epitopes were recognized, when compared with alum-adsorbed HIV-1 gp160D formulation. Low-level, antigen-specific proliferative responses to HIV-1 recombinant gp160 were induced by either vaccine formulation. Proliferative responses were induced by a sham challenge with soluble recombinant HIV-1 gp160 for all of the animals that had been vaccinated. However, those that received the HIV-complete vaccine formulation containing QS-21 responded significantly better. These data demonstrated that the QS-21 adjuvant augmented both antibody responses and cell-mediated immunity and established immunological memory. The potent adjuvant activity and lack of toxicity suggest that this adjuvant should be safe and effective for use in HIV-1 vaccines.

Tags: Animal; Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Adjuvants, Immunologic; *AIDS Vaccines; *Gene Products, env

--Immunology--IM; *HIV-1--Immunology--IM; *Protein Precursors--Immunology --IM; *Saponins--Immunology--IM; *Vaccines, Synthetic; HIV Antibodies --Biosynthesis--BI; Lymphocyte Transformation; Macaca mulatta--Immunology --IM; Recombinant Proteins--Immunology--IM
CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Gene Products, env); 0 (HIV envelope protein gp160); 0 (HIV Antibodies); 0 (Protein Precursors); 0 (Recombinant Proteins); 0 (Saponins); 0 (Vaccines, Synthetic); 141256-04-4 (QS 21)

13/5/11 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08028393 92166393
Saponin adjuvant enhancement of antigen-specific immune responses to an experimental HIV-1 vaccine.
Wu JY; Gardner BH; Murphy CI; Seals JR; Kensil CR; Recchia J; Beltz GA; Newman GW; Newman MJ
Cambridge Biotech Corporation, Worcester, MA 01605.
J Immunol (UNITED STATES) Mar 1 1992, 148 (5) p1519-25, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9206
Subfile: AIM; INDEX MEDICUS
The adjuvant activity of a single highly purified saponin from the soap bark tree Quillaja saponaria was evaluated by using it as a component in an experimental vaccine containing rHIV-1 envelope protein (HIV-1 160D) adsorbed to alum. BALB/c mice immunized with experimental vaccine formulations containing the saponin adjuvant QS-21 produced significantly higher titers of antibodies than mice vaccinated with only the alum-adsorbed HIV-1 160D. Potent amnestic antibody responses to HIV-1 viral proteins were also induced. Ag-specific proliferative responses to recombinant proteins and to three variants of HIV-1 were significantly increased using QS-21 as an adjuvant. Alum-adsorbed HIV-1 160D failed to induce measurable proliferative responses to inactivated HIV-1 viruses, but group-specific proliferative responses were raised when the QS-21 adjuvant was used in the vaccine formulation. MHC class I restricted CTL specific for the immunodominant V-3 loop were induced but only when the QS-21 adjuvant was included in the vaccine formulation. The production of serine esterase by Ag-activated splenic mononuclear cells, indicating the maturation of precursor CTL, was used as a secondary measure of CTL activity, and this response was also increased. The specificity of antibody responses was not significantly broadened using QS-21; the adjuvant increased the immune recognition of epitopes throughout the HIV-1 glycoprotein 160. However, the specificity of the proliferation and serine esterase responses was broadened, suggesting that the QS-21 augmented cell-mediated immune responses specific for epitopes outside of the V-3 loop. Additionally, the QS-21 adjuvant appeared to induce recognition of weakly immunogenic epitopes that were not recognized using only alum-adsorbed HIV-1 160D. The ability of QS-21 to augment both antibody and cell-mediated immune responses suggests that this adjuvant could be a valuable component in subunit vaccines.
Tags: Animal; Female
Descriptors: *Adjuvants, Immunologic--Pharmacology--PD; *AIDS Vaccines --Immunology--IM; *Gene Products, env--Immunology--IM; *HIV-1--Immunology --IM; *Protein Precursors--Immunology--IM; *Saponins--Pharmacology--PD; *Vaccines, Synthetic--Immunology--IM; Esterases--Biosynthesis--BI; HIV Antibodies--Analysis--AN; Lymphocyte Transformation; Mice; Mice, Inbred

BALB C
CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Gene Products, env); 0 (HIV envelope protein gp160); 0 (HIV Antibodies); 0 (Protein Precursors); 0 (Saponins); 0 (Vaccines, Synthetic)
Enzyme No.: EC 3.1. (Esterases); EC 3.1.- (serine esterase)

13/5/12 (Item 1 from file: 377)
DIALOG(R)File 377:Derwent Drug File

00510992 DERWENT ACCESSION NUMBER: 92-51976
Saponin.
Campbell J B; Peerbaye Y A
Res.Immunol. 143, No. 5, 526-30, 1992
CODEN: RIMME5 ISSN: 0923-2494 LANGUAGE: English RECORD TYPE: Abstract

REPRINT ADDRESS: Department of Microbiology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada.

ABSTRACT:
The use of Quillaja saponins (SP) as immunological adjuvants is reviewed. The use of SP has been limited because of toxicity, but recent studies with purified SP (e.g. QS-7, QS-17, QS-18, QS-21) demonstrate that adjuvant activity is not necessary associated with toxicity. SP adjuvants probably mediate their effects by several nonspecific and specific mechanisms. Possible applications of SP in vaccine (HIV, rabies) are detailed.

SPECIAL FEATURES: 1 Fig. 1 Tab. 33 Ref.
COMMON TERMS:
REVIEW --FT; MODE-OF-ACT. --FT; IN-VIVO --FT; IMMUNOSTIMULANT --FT; MOUSE --FT; ADJUVANT --FT; LAB.ANIMAL --FT
LINK TERMS:
01; QUILLAJA-SAPONIN --PH; MAIN-TOPIC --FT; ADJUVANTS --FT; IMMUNOSTIMULANTS --FT; QUILLAJSA --RN; PH --FT
02; RABIES-VACCINE --PH; OVALBUMIN --PH; INTERFERON-GAMMA --PH; RABIES-VIRUS --FT; PLANT-SUBSTANCE --FT; TOX. --FT; DRUG-APPL. --FT; P.O. --FT; PARENTERAL --FT; VACCINE --FT; IMMUNE-RESPONSE --FT; CELL-MEDIATED --FT; HUMORAL --FT; IGG1 --FT; IGG2A --FT; IGG2B --FT; IGE --FT; DOSAGE --FT; SP. --FT; THYMOCYTE --FT; ANTIBODY-RESPONSE --FT; RHABDOVIRUS --FT; VIRUS --FT; IMMUNITY --FT; IMMUNOGLOBULIN --FT; IMMUNOGLOBULIN --FT; IMMUNOGLOBULIN --FT; IMMUNOGLOBULIN --FT; LYMPHOCYTE --FT; PH --FT; AE --FT

SECTION HEADINGS: Immunological (20); Toxicology (34); Biol. Response Modifiers (50); Reviews (69)
THEMATIC GROUPS: M (Microbiology)
?e au=prieels, john p.

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E3	2	AU=PRIEELS, RENE
E4	2	AU=PRIEELS,J.-P.
E5	1	AU=PRIEELS,J.P.
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E7	4	AU=PRIEFER A
E8	1	AU=PRIEFER A.
E9	13	AU=PRIEFER B

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 14/5/1      (Item 1 from file: 76)
DIALOG(R)File  76:Life Sciences Collection
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546474
  Agglutinability of Micrococcus luteus by human lactoferrin upon lysozyme
action.;
  Perraudin,J.P. ; Prieels,J.P.
  (Lab. Chim. Gen. I, Fac. Sci., Univ. Libre de Bruxelles, B-1050 Brussels,
Belgium)
  Arch. Int. Physiol. Biochim. ; 88(1), B43-B44 1980 ;
  Language: English
  Document Type: Journal article-original research
  Subfile: 02  Microbiology Abstracts B Bacteriology; ;
  Descriptors: Micrococcus luteus; man; infection; lactoferrin; interaction
; lysozyme; antibacterial activity; agglutination
  Section Heading Codes: 02602; 02593X
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